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TRIP REPORT TO KIEV AND MINSK - JUNE 1998

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This was my first trip to Kiev and Minsk as part of the Columbia-NCI Contract to study the long term effect of the Chernobyl disaster on the thyroid gland of exposed children. My comments will be confined to Cytology and Pathology, emphasizing cytology.

Kiev, Ukraine:

The Cytology Laboratory at the Institute of Endocrinology and Metabolism is referred to as the "Laboratory of Functional Diagnosis". The Laboratory head is Dr. Yu.M. Bozhok. There are four other cytologists: Dr. Anna Zelinskaya, Dr. Tonya Khorozhenko, Dr. Anna Uscimenko and Dr. Delina Kulinichenko. Institute of Endocrinology and Metabolism, Vyshgorodskaya Str. 69, Kiev - 254114, Ukraine, Phone (044) 431-02-96 or 431-04-22.

Cytologists' background

Ukranian cytologists' training consists of a five year University Program, after High School, resulting in a degree of Doctor in Biology. The five years of training include basic sciences, biology, anatomy, histology, and cytology. This amount of training is equivalent to that received by cytotechnologists in the United States: a four year college degree plus one year of training in cytology including anatomy and histology. No medical doctor or pathologist is involved in slide review or laboratory management.

Laboratory supervision

The senior cytologist and supervisor, Dr. Bozhok, has a wealth of experience in thyroid cytology and has compiled an atlas of typical diagnostic findings and their features; this atlas has been copyrighted and published by Germans involved in Chernobyl aid and distributed to other Ukranian Cytology Laboratories.

Exciting technical, cytodiagnostic, and prognostic scientific research is being carried out in Dr. Bozhok's laboratory, although not as a part of the Chernobyl cohort study.
Case volume

The number of patients with fine needle aspirations is between 1300 and 3000 cases per year; roughly 10 to 15 cases per day, 4 days per week. When multiple nodules are aspirated they are sublabelled A, B, C, D, etc, but not counted as separate cases. The lab receives roughly 6 to 10 slides per case. It is not clear whether inadequate slides were discarded or were saved and counted. The log book for a random day included 12 patients, 79 slides. A different two day period combined had 198 slides.

Although I did not have a chance to review any of the cytology cases from the Chernobyl Cohort project, I was shown a tabulation of the case numbers with the following results:

The number of FNA's of thyroid in 1997 was 1546 adults and 352 children, however, only two cohort patients have had fine needle aspirates since the study began. The number of aspirates performed in 1997 is higher than in prior years; in 1995 and 1996 combined, there were thyroid FNA's on 2129 adults and 344 children, hence the number of children per year had at least doubled in 1997. The numbers are predicted to continue to increase because of Chernobyl disaster effect, screening projects, increased number of

sonographers (1 in 1984, 2 in 1994, and 4 in 1998), improving sonographic equipment, detection and aspiration of smaller nodules. These factors will contribute to the increase in number of positive fine needle aspiration biopsy results, however it is not yet determined whether all of these tumors detected are of prognostic significance.

Cytology laboratory Workflow and equipment

The Cytology laboratory work distribution is set up so that one of the four cytology Doctors screens and diagnoses cases one day each week. Another cytologist assesses adequacy one day per week, and another cytologist stains slides one day per week. Aspirates are done only four days per week.

The laboratory has two good clinical Leica microscopes, one of which is used exclusively for screening. The other, has a photomicroscopy unit donated by Japanese benefactors. A third "adequate" microscope is set up in the ultrasonography room for immediate assessment of adequacy of fine needle aspiration biopsies. Dr. Bozhok would like an additional microscope for clinical use, especially with a fluorescence unit for special stains. I am unclear as to why the second Leica microscope is not in clinical use; it is locked in a separate room. I will look into this on my next visit.

Adequacy assessment

A cytologist assists at the ultrasound guided fine needle aspiration biopsies and assesses adequacy based on microscopic examination of unstained slides. The assessment of adequacy based on unstained slides is new to me but seems feasible after a demonstration; the condensor or diaphragm is lowered or closed. The current cytology staff appears comfortable with this approach, hence it is unnecessary to impose Diff Quik staining for the immediate assessments (the method used in the US). The only means I have to verify that this technique works is that their reported rate of insufficient specimens is in the range of 1 to 4%, which is impressively low. I have not seen whether there are specific guidelines in use for their assessment of adequacy.

Definition of diagnostic categories

It would be valuable to specify cytologic diagnostic categories and their criteria in writing.

Criteria for determining who performs the aspirate

It is my impression that only the sonographers, not the endocrinologists, perform fine needle aspirates, even if the nodules are palpable. If both are performing aspirates, it is important to specify how the decision as to who does the aspirate is made.

Criteria for determining surgical intervention

All detected nodules are aspirated, in spite of the fact that the protocol indicates that in adults, only nodules greater than or equal to 1.0 cm in diameter, and in children, only those 0.5 cm. or greater in diameter should be aspirated. This protocol criterion should be changed to reflect the actual practice.

It would be valuable to document the criteria used by endocrinologists to recommend surgery. Even if the decision is multifactorial, it is useful to specify the decision making criteria as it pertains to fine needle aspirate diagnoses i.e. the algorythm. It will be of interest to determine how often a second cytologic review is performed, particularly on indeterminate cases and how discrepant opinions are reconciled. The reported sensitivity of 98% is high. I assume inadequate cytologic specimens are excluded; the method of arriving at the sensitivity should be specified.

Quality Control / Quality Assurance

I doubt histologic diagnoses are used to revise cytologic diagnoses, but this would be important to know as it would change the sensitivity, specificity, positive predictive value, and negative predictative value. The negative cytologic diagnoses are not reviewed even randomly or spot checked by a second cytologist. This would be a valuable quality assurance measure. Cytologists do check the written histologic diagnosis (not the slides) and use the histologic diagnosis as a "gold standard" and as the basis for calculating sensitivity of cytologic diagnosis, a good first step toward the QA goal.

Quality assurance and quality control limit the reliability of the data. For the cohort, it will be necessary to review both positive and negative cytology cases.

MINSK: BEL-AM PROJECT

Cytologists in Minsk are biologists referred to as Laboratory Doctors, as in Kiev. There is one cytologist involved with the cohort study, Dr. Yelena Kapanovitch. Four other "thyroid experts" with the same "U.S. cytotechnologist" level training also work at Dr. Dmidchik's laboratory. I did not meet the other 4, but I was told that they were all "senior." They are all at the same level without a designated cytology supervisor; Dr. Dmidchik, a surgeon, is the professional in charge.

Thus far there have been 9 fine needle aspiration biopsies, consisting of 42 slides, on cohort children. I believe these slides are all from Minsk, but do not know how many were repeated in, or derived from, Aksakachina. Also, these case and slide numbers may include patients screened now, but with prior FNA'S dating back to 1995. I need information regarding the cytology program at Aksakovchina.

Will all cohort patients with nodules detected now, and with a history of fine needle aspiration in the past, need slide review and a form?

No pathologist has reviewed or is involved in assessing the cytology material. No followup is performed by the cytologist or pathologist as to the diagnosis of the other's pathomorphologic studies. No calculation of sensitivity or positive predictive value is being performed. No review of negative cases is performed. Review of even a sample of negative cases would be a good quality assurance measure. No report of percentage inadequate cases is given. No written criteria for diagnostic classification has been made available to me. No cytologist is available for immediate assessment. This is a problem according to the ultrasonography doctors and endocrinologists. I am not sure whether endocrinologists sometimes aspirate palpable nodules. It seems that the endocrinologists and ultrasonographers want to be able to assess adequacy themselves, the implication being that the adequacy rate is low.

The ultrasonographers and endocrinologists asked for a cytology presentation from me on future visits to discuss assessment of adequacy, what the cytologist can and cannot tell, and basic cytodiagnostic criteria for thyroid cancer.

I need approixmately 2 full days to review cytologic cases, including both negatives and positives among cohort patients, to assess the quality of the fine needle aspirations and aspirators. Before this occurs it is necessary for me to have the cohort's diagnostic forms translated into English- including diagnoses, conclusions, and histopathologic diagnoses- before my arrival, in writing. This would also allow me to determine whether the cytologist is using the forms correctly, enabling me to get and give feedback as to whether the forms are appropriate, prior to the 1 year cut-off point for the alteration of forms.

It would be valuable for me to visit Aksakachina or to at least find out its role in the cytologic workup. I am interested to find out the validity of the complaint attributed to the doctors in Aksakachina that fine needle aspirations should not be done anywhere besides there!

Suggestions and proposed milestones for cytology laboratory (Ukraine and Belarus):

1. Create written criteria for specimen adequacy, diagnostic categories, and instructions for filling in forms. I will provide guidelines from Papanicolaou Society.

2. Create a log of cohort cases, fine needle aspiration biopsy diagnosis and histology diagnosis directly in the laboratory and in DCC.

3. Establish a system for performing and documenting secondary review of cohort cases' slides even when the initial diagnosis has been "non-informative".

4. Mention whether discarding slides is done prior to, or subsequent to, recording the number of slides.

5. Change the minimum size requirement for the FNA of thyroid nodules to reflect what is being done.

6. Clarify the role of Aksakochina in the sonographic and FNA evaluation and re-evaluation of Bel-Am cohort patients.

7. Determine the frequency with which FNA's are performed by endocrinologists rather than sonographers. Based on specimen adequacy rates: determine whether endocrinologists require additional training and/or credentialing, or whether all cohort aspirates should be done by sonographers.